REMARKS:

Applicant has carefully studied the nonfinal Examiner's Action and all references cited therein. The amendment appearing above and these explanatory remarks are believed to be fully responsive to the Action. Accordingly, this important patent application is now believed to be in condition for allowance.

Applicant responds to the outstanding Action by centered headings that correspond to the centered headings employed by the Office, to ensure full response on the merits to each finding of the Office.

Drawings

The Office has objected to the drawings identifying figures 1, 4 and 6 as being of poor quality. Additionally, figures 1 and 4 are identified in the specification as color photographs and the Office has noted that not color photographs have been submitted.

Substitute drawings have been presented along with this Amendment. Figures 1, 4 and 6 have been canceled. The remaining figures have been renumbered and appropriate correction to the specification has been presented in this amendment.

Claim Rejections – 35 U.S.C. § 112

Applicant acknowledges the quotation of 35 U.S.C § 112, second paragraph.

Claims 21-23 stand rejected under 35 U.S.C § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

More specifically, independent claim 21 stands rejected for reciting a "formula" that contains a symbol "~", which the Office has stated usually means "proportional" or "approximately equal" and as such, it is not clear what the "~" symbol means in the formula. The Applicant respectfully traverses the finding of the Office.

In statistics, the tilde symbol, "~" is frequently used to mean "has the distribution (of)", for instance, $X \sim N(0,1)$ means the stochastic (random) variable X has the distribution $N(0,1)$ (the standard normal distribution). If X and Y are stochastic variables then $X \sim Y$ means X has the same distribution as Y.

The Office has additionally rejected claim 21 due to inconsistencies between the formula presented in claim 21 and the specification. Applicant thanks the Office for identifying this discrepancy. Claim 21, claim 22, and the specification have been amended to recite the same formula as originally intended by the invention.

The Office states that the term "σ" used in the formula of claim 21 is not defined in the specification. The symbol sigma, "σ^2", is well known in the field of statistical analysis to refer to the variance of a probability distribution, such as the distribution $N[\cdot]$ in the formula of claim 21.

Regarding claim 22, the Office states that the expression $N[\cdot]$ is not recited in parent claim 21 and that, as such, there is no antecedent basis for the term, thereby rendering claim 22 indefinite. Applicant respectfully traverses the finding of the Office.

The expression "$N[\cdot]$" as used in claim 22 is intended to reference the expression "$N\left[f\left(t_{il},\alpha_{mi},\beta_{lj},\gamma_{ml}\right),\sigma^2\right]$" from claim 21. This symbolism is commonly used in statistics as a shorthand method of referencing a particular distribution without having to listing each of the parameters of the distribution. The language of claim 22 has been amended to make it clear that the dependent claim is intended to limit the distribution $N[\cdot]$ to a Gaussian distribution.

For the reasons indicates above, Applicant believes that amended claims 21-23 are definite and particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections – 35 U.S.C. § 103

Applicant acknowledges the quotation of 35 U.S.C § 103(a).

Claims 21-23 stand rejected under 35 U.S.C § 103(a) as being unpatentable over Alon, *PNAS*, 96:6745-6759 (1999), in view of Lazaridis, E., Discrimination and classification using conditionally independent marginal mixtures, *A Dissertation Thesis*, Chicaco, The University of Chicago, Illinois, December 1994, and further in view of Skene, *Statistics in Medicine*, 11:2111-2122 (1992).

The method in accordance with the present invention identifies latent, or unobservable, properties of objects within a given sample or population, which properties are then useful to determine relationships and, potentially, classification schemes as stated in the Field of the Invention of the specification as originally filed.

Claim 21 includes the step of identifying latent classes of the genes in the first direction, and latent classes of cells or tissue samples in the second direction according to a specific formula as defined by the claim.

The method described by Alon et al. does not identify latest classes of genes from a matrix in a first direction and latest classes of cell or tissue samples from a matrix in a second direction as disclosed and claimed by the present invention. By contrast, the method described by Alon utilizes a clustering approach to detect groups of correlated genes and tissues from a data set. This is not equivalent to the method as disclosed and claimed by the present invention.

Additionally, claim 21 recites the step of, "calculating the likelihood that each gene is a member of each identified latent class for the first direction, while also calculating, simultaneously or serially, the likelihood that each cell or tissue sample is a member of each identified latent class for the second direction". As such, the present invention utilizes a probabilistic structure to identify and quantify data patterns. Accordingly, the present invention assigns to individual genes probabilities (i.e. likelihood) of membership in specific patterns, allowing one to quantify uncertainty associated with allocating elements among set of interpretable categories, as described at paragraph [0068].

Alon et al. does not describe calculating the likelihood that each gene is a member of each identified latent class as disclosed and claimed by the present invention. Alon et al. does

not describe calculating the "probability", or "likelihood" that a gene is a member of a particular class, but rather, Alon describes separating genes into distinct clusters.

As described by Along at pg. 6748, detecting groups of correlated genes and tissues is accomplished utilizing a clustering approach to the data set in which genes are near each other on the "gene tree" if they show a strong correlation across experiments, and tissues are near each other on the "tissue tree" if they have similar gene expression patterns. To this end, Alon et al. describes separating the set of objects into two groups, then separating each group into two subgroups, and so on, until all the objects are arranged on a binary tree. Clearly, this technique requires that the object be placed into one or another category (i.e. binary) based on observable characteristics. Alon, does not describe a method whereby the likelihood of the objects belonging to a particular group is addressed. Alon does not describe a method incorporating likelihood and probability of belonging to a latent class as described and claimed by the present invention.

For the reasons cited above, Applicant believes that amended independent claim 21 is patentable over Alon in view of Lazaridis and Skene and is believed to be in condition for allowance.

Claims 22-23 are dependent upon claim 21, and are therefore allowable as a matter of law.

If the Office is not fully persuaded as to the merits of Applicant's position, or if an Examiner's Amendment would place the pending claims in condition for allowance, a telephone call to the undersigned at (727) 507-8558 is requested.

Very respectfully,

SMITH & HOPEN

By: [signature]

Dated: November 23, 2005
Reg. No. 53,296

Michael M. McGaw
15950 Bay Vista Drive, Suite 220
Clearwater, FL 33760
(727) 507-8558
Attorneys for Applicant

CERTIFICATE OF MAILING

(37 C.F.R. 1.10)

I HEREBY CERTIFY that this correspondence is being deposited with the United States Postal Service in an envelope as "Express Mail Post Office to Addressee," mailing Label No. EV770341938, addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on November 23, 2005.

Date: **November 23, 2005**

April Turley

IN THE DRAWINGS:

Please replace the drawings with the replacement drawing set presented with this amendment effectively deleted figures 1, 4 and 6 and renumbering the remaining drawings as required.

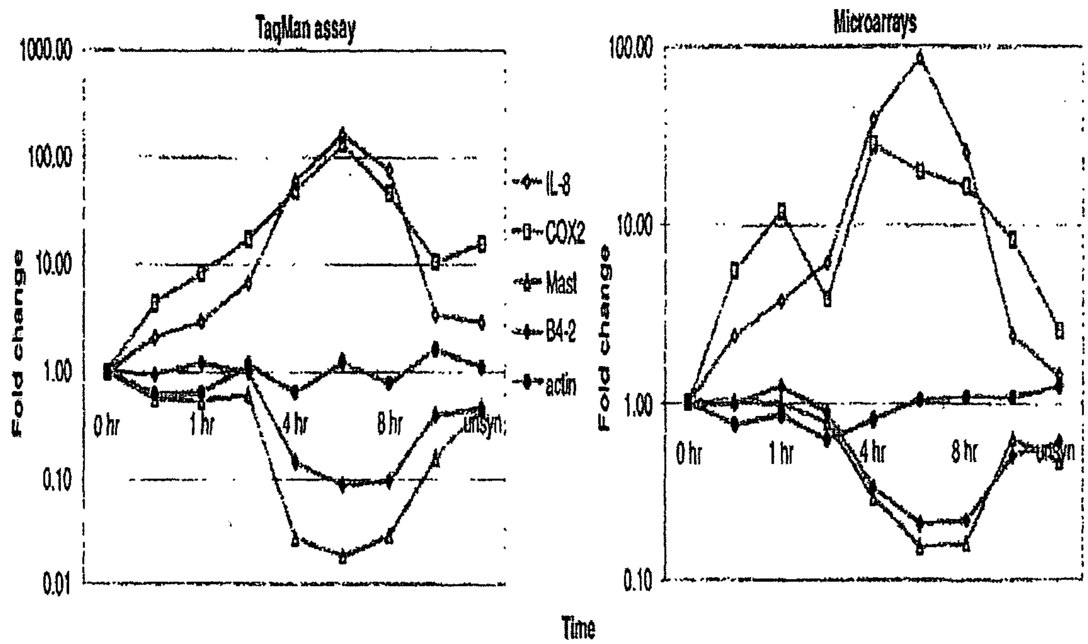

TaqMan assay
1000.00
100.00
10.00
1.00
0.10
0.01
Fold change
0 hr
1 hr
4 hr
8 hr
unsyn
IL-8
COX2
Mast
B4-2
actin
Microarrays
100.00
10.00
1.00
0.10
Fold change
0 hr
1 hr
4 hr
8 hr
unsyn
Time

FIGURE ~~2~~ 1

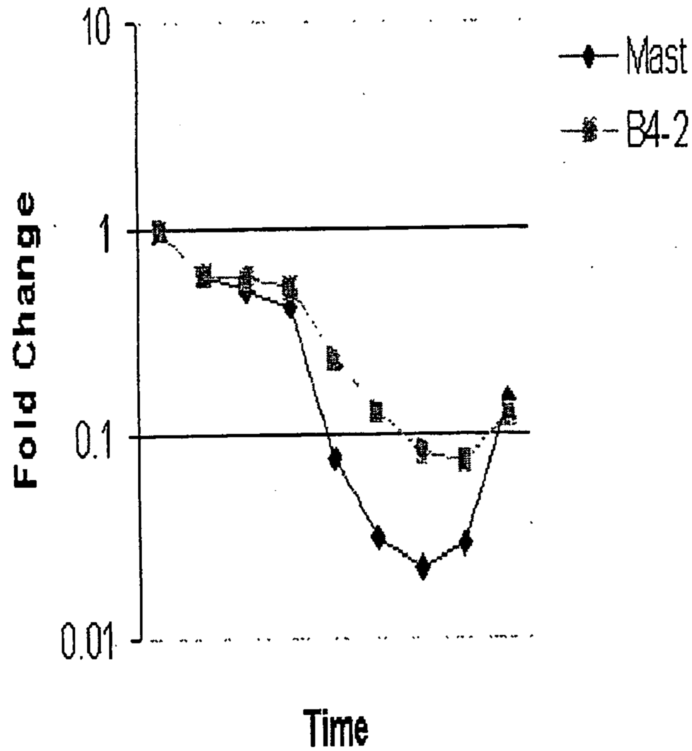


FIGURE ~~3~~2

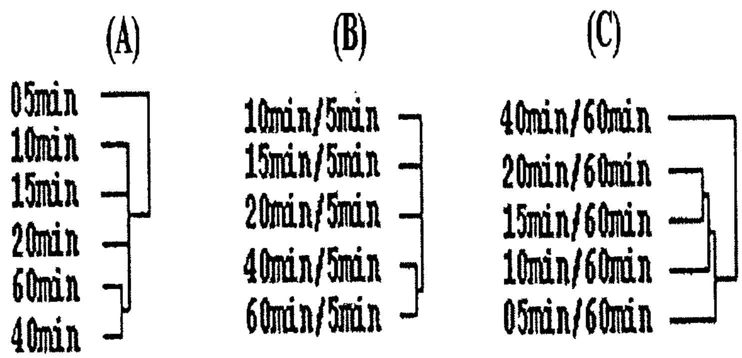

(A)
05min
10min
15min
20min
60min
40min
(B)
10min/5min
15min/5min
20min/5min
40min/5min
60min/5min
(C)
40min/60min
20min/60min
15min/60min
10min/60min
05min/60min

FIGURE ~~5~~3

ClonTech Filter

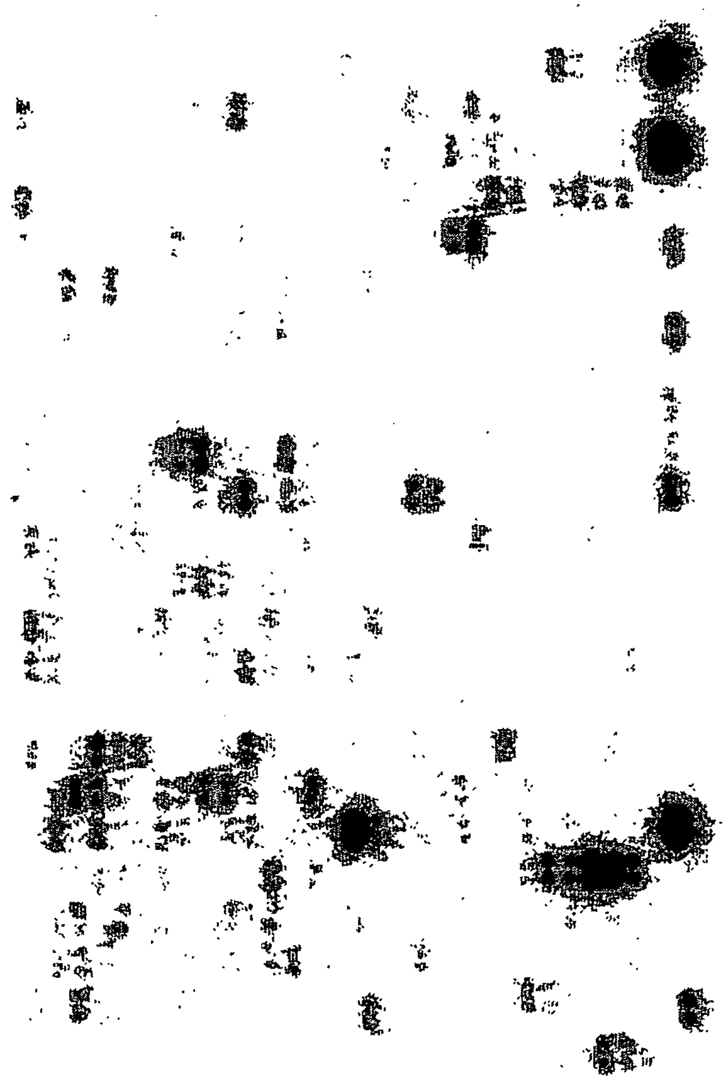


Figure ~~7~~ 4

NEN Micromax Slide

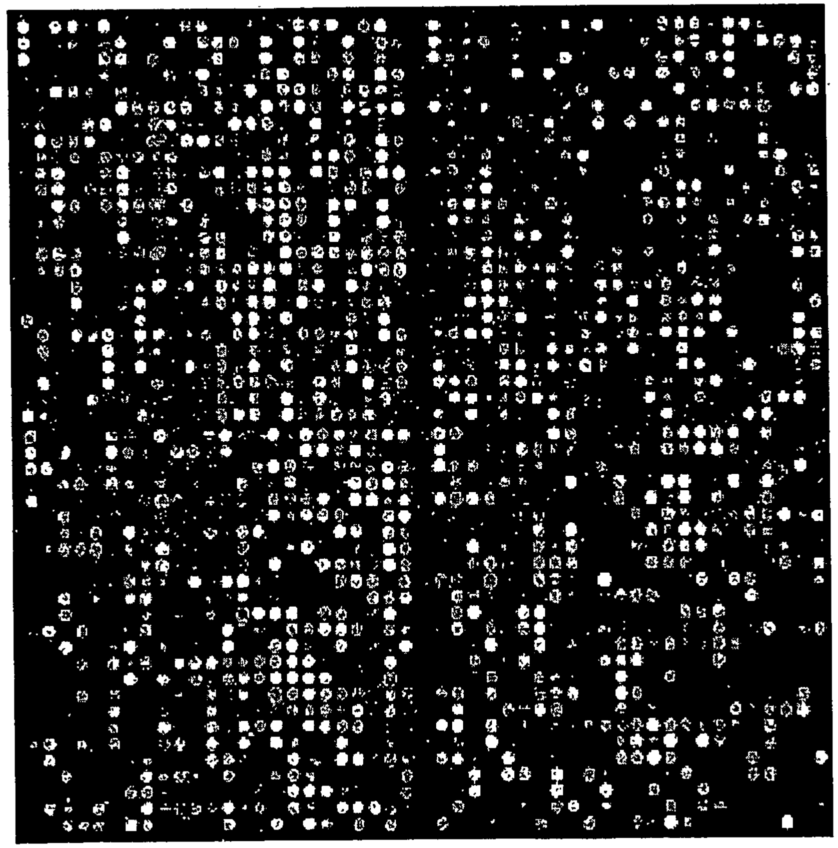


Figure ~~8~~5

Affymetrix System

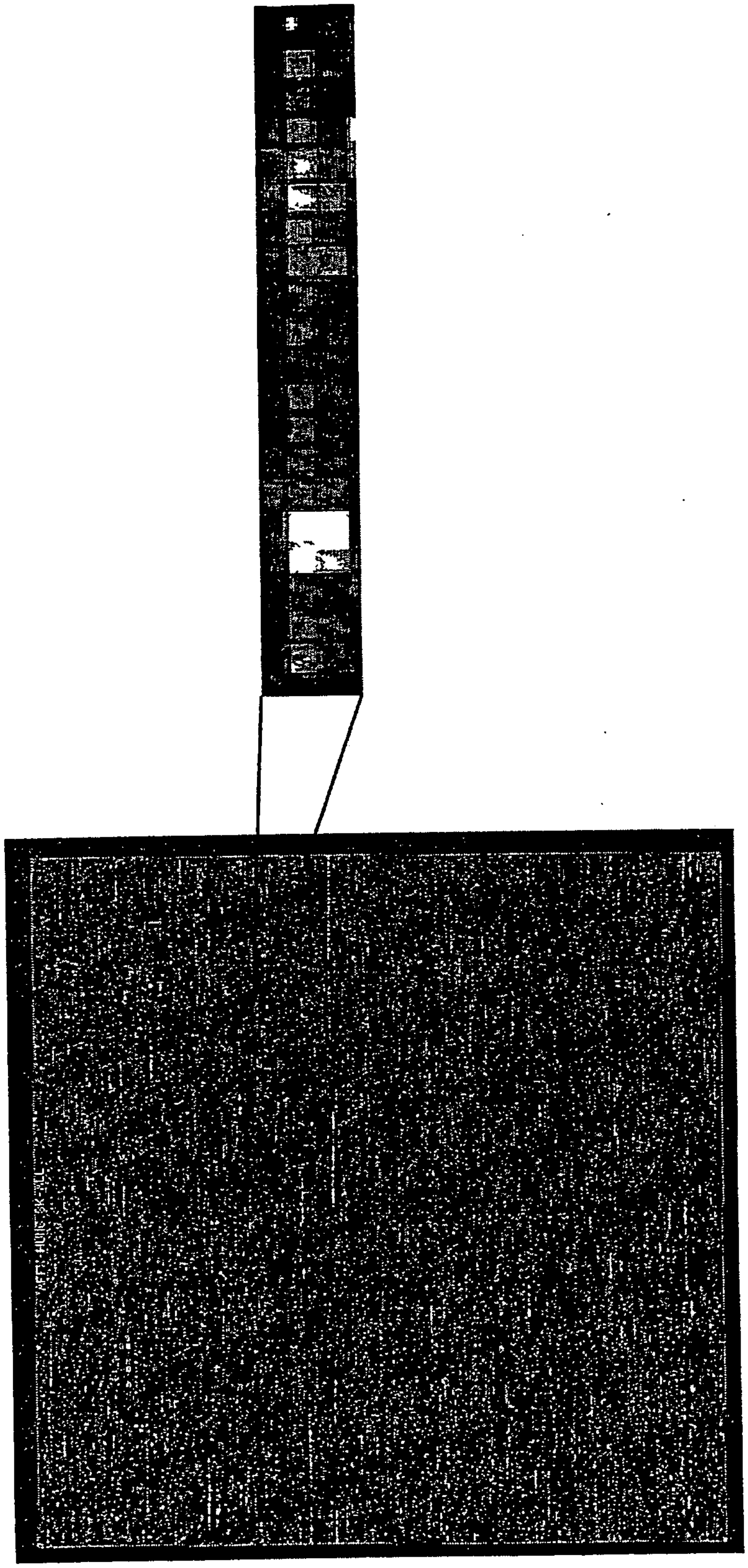


Figure ~~0~~ 6

Assignment of 62 Normal and Cancer Tissues Among the Five Classes

	Latent Tissue Class				
	I	II	III	IV	V
Cancer	1	30	5	2	2
Normal	16	2	3	1	0

FIGURE ~~10~~ 7

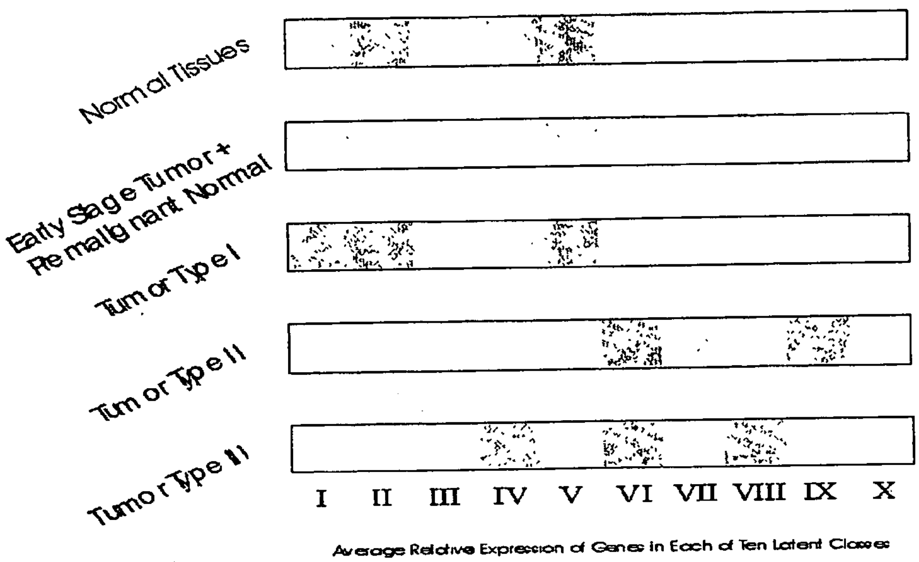

Normal Tissues
Early Stage Tumor + Premalignant Normal
Tumor Type I
Tumor Type II
Tumor Type III
I II III IV V VI VII VIII IX X
Average Relative Expression of Genes in Each of Ten Latent Classes

FIGURE ~~1~~ 8

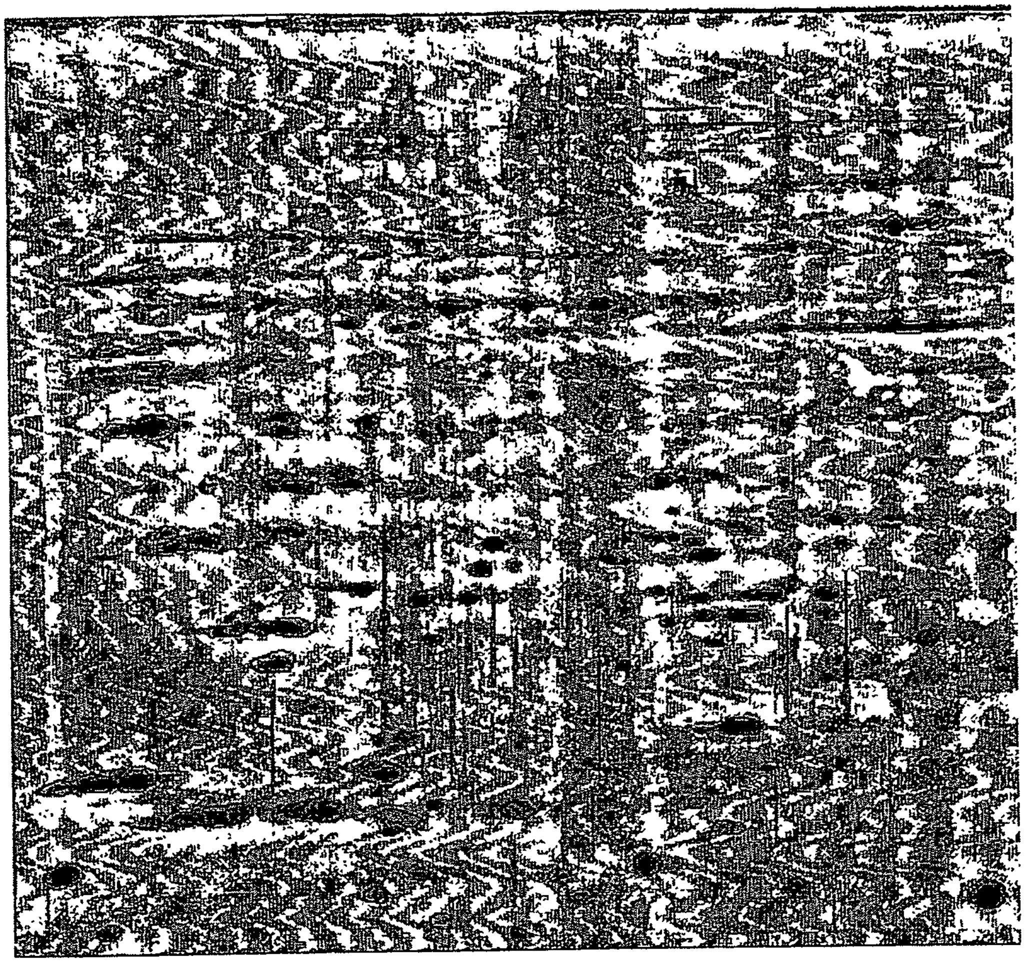


FIGURE ~~12~~ 9

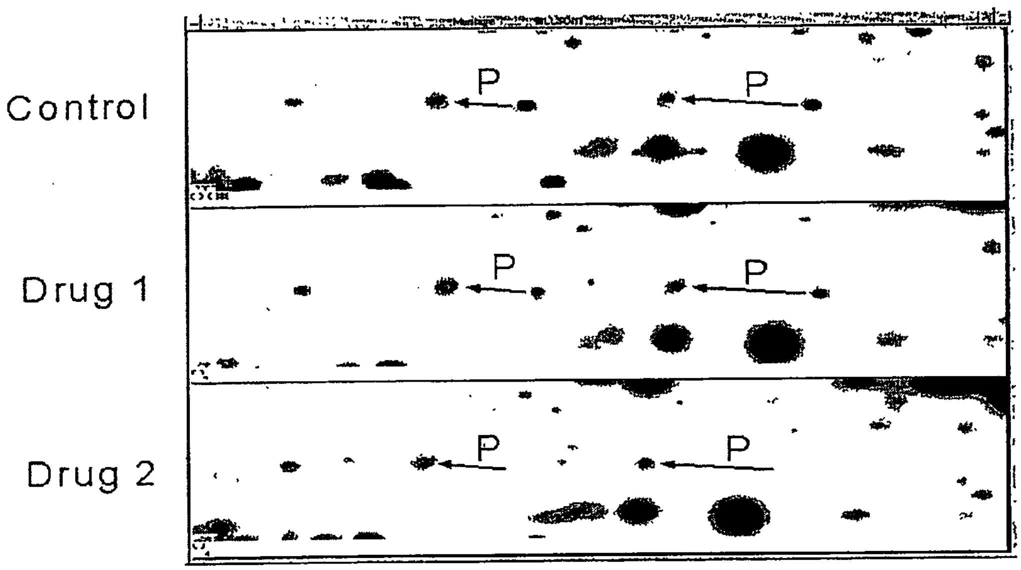


FIGURE ~~18~~ 10

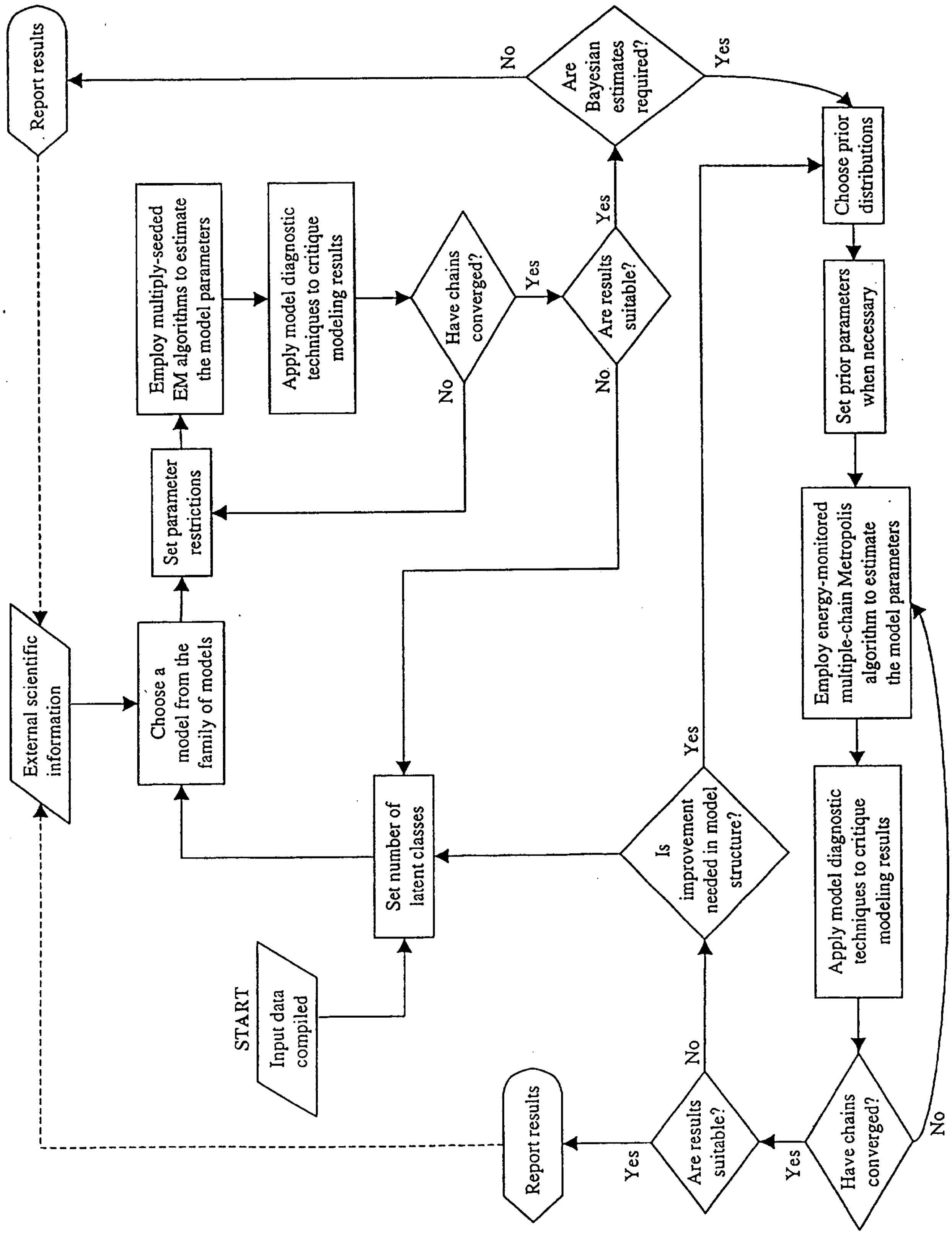
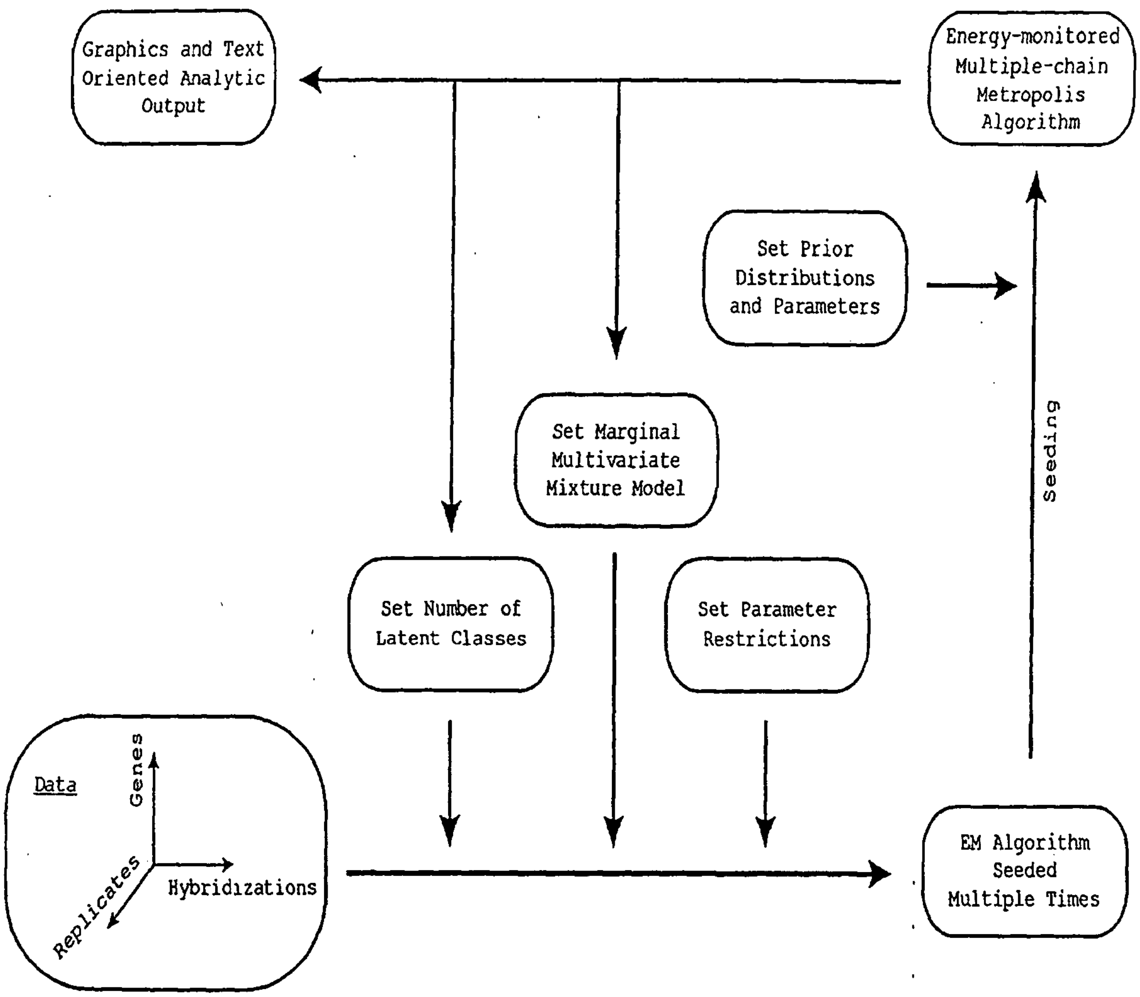

START
Input data compiled
Set number of latent classes
External scientific information
Choose a model from the family of models
Set parameter restrictions
Employ multiply-seeded EM algorithms to estimate the model parameters
Apply model diagnostic techniques to critique modeling results
Have chains converged?
Yes
No
Are results suitable?
Yes
No
Are Bayesian estimates required?
No
Yes
Report results
Choose prior distributions
Set prior parameters when necessary
Employ energy-monitored multiple-chain Metropolis algorithm to estimate the model parameters
Apply model diagnostic techniques to critique modeling results
Have chains converged?
No
Yes
Are results suitable?
Yes
No
Report results
Is improvement needed in model structure?
Yes

Figure ~~14~~ 11

Figure ~~13~~ 12: Illustration of the process employed to calculate estimates of parameters from Bayesian statistical models using a sampling approach



This example illustrates data with 3 margins.

Figure ~~16~~ 13: Illustrated application of multichain monitored algorithms employed to discover solution for Bayesian statistical models